

research aims at the design of aminoglycosides capable of evading efflux pumps and efflux pump inhibitors (Opperman and Nguyen 2015; Venter et al. 2015).

1.3 Development of New AGAs: The Potential of Glycomics

Outstanding problems of AGAs are related with their efficacy due to increasing antibiotic-resistant bacteria and aminoglycoside inherent toxicity. The rational design for novel AGAs will have to consider (i) the ability of the drug to bind strongly and specifically to the bacterial therapeutic target and (ii) the lack or weak binding to resistance- and toxicity-causing enzymes. The available structural data involving aminoglycoside-bound rRNA molecules and details of the resistance mechanisms with insights obtained from X-ray structures of AMEs has made AGAs' rational design possible. This topic has been extensively reviewed (Thamban Chandrika and Garneau-Tsodikova 2018). A relevant example is plazomicin (ACHN-490, Achaogen Inc.), a semisynthetic *N*-acylated AGA of the 4,6-disubstituted deoxystreptamine (4,6-DOS) type (Aggen et al. 2010), which is in clinical development as a new antibacterial agent (Table 1.1). The evidence shows that ACHN-490 targets the bacterial ribosome with high binding affinity and could be resistant to most of aminoglycoside resistance-causing enzymes (Endimiani et al. 2009; Aggen et al. 2010; Armstrong and Miller 2010; Labby and Garneau-Tsodikova 2013; López-Díaz et al. 2016).

In recent decades, the study of carbohydrates (or glycans) and their derivatives has emerged as a challenging area providing new avenues of research at the interface of chemistry and biology. The advances in glycomic approaches have helped to elucidate biological functions of carbohydrates. Development of methods for chemical or chemoenzymatic synthesis of carbohydrates (Boltje et al. 2009; Muthana et al. 2009) and for their analysis by NMR (Kato and Peters 2017) or mass spectrometry (Kailemia et al. 2014) has contributed to these advances, as well as the development of high-throughput methods for interaction studies, such as carbohydrate microarrays (Rillahan and Paulson 2011; Palma et al. 2014). The convergence of these methodologies is leading glycomics at the forefront of research to design glycan mimetics, offering the opportunity to develop drugs, including aminoglycosides targeting diverse structures of RNA (Thamban Chandrika and Garneau-Tsodikova 2018 and references therein). In the subsections below, carbohydrate chemistry and microarray technology are briefly highlighted as powerful approaches toward development of new AGAs and analysis of aminoglycoside target interactions.